AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application. Please amend claim 5 as indicated below.

1. (Original) A method of diagnosing skin cancer in a patient comprising:

providing a tissue sample from a patient suspected of having skin cancer; and

determining whether cells in said tissue sample express MrgX2, wherein expression of MrgX2 indicates that the patient has skin cancer.

2. (Original) The method of Claim 1, wherein the skin cancer is melanoma.

3. (Original) The method of Claim 1, wherein the tissue sample comprises skin cells.

4. (Original) The method of Claim 1, wherein MrgX2 expression is determined by contacting the tissue sample with an antibody that specifically binds MrgX2 and determining if the antibody binds to the tissue sample.

5. (Currently amended) The method of Claim 4, wherein the antibody is a monoclonal antibody.

6. (Original) The method of Claim 4, wherein the antibody is detectably labeled.

7. (Original) The method of Claim 6, wherein the antibody is labeled with a radioactive label.

8. (Original) The method of Claim 6, wherein the antibody is labeled with a fluorescent label.

9. (Withdrawn) The method of Claim 1, wherein MrgX2 expression is determined by contacting the sample with a nucleic acid probe that is complementary to a portion of the MrgX2 nucleic acid of SEQ ID NO: 3 and determining if the probe binds to the tissue sample.

10. (Withdrawn) The method of Claim 9, wherein the probe is detectably labeled.

11. (Original) The method of Claim 1, wherein said MrgX2 has the amino acid sequence of SEQ ID NO: 4

12. (Withdrawn) A method of diagnosing melanoma in a patient comprising:

obtaining a tissue sample from the patient;

preparing RNA from the tissue sample;

contacting the RNA with a nucleotide probe that is capable of hybridizing to the MrgX2 nucleotide sequence of SEQ ID NO: 3 under stringent conditions; and

determining binding of the nucleotide probe to RNA in the sample.

13. (Withdrawn) The method of Claim 12, wherein the nucleotide probe is detectably labeled.

14. (Withdrawn) The method of Claim 12, wherein the RNA is mRNA.

15. (Withdrawn) The method of Claim 12, wherein the RNA is total RNA.

16. (Withdrawn) The method of Claim 12, wherein said tissue sample comprises skin cells.

17. (Original) A method of diagnosing melanoma in a patient comprising:

obtaining a tissue sample from the patient;

isolating protein from the tissue sample;

contacting the protein with an antibody to MrgX2; and

determining binding of the antibody to the protein, wherein specific binding of said antibody to the protein is indicative of melanoma.

18. (Original) The method of Claim 17, wherein the antibody is a monoclonal antibody.

19. (Original) The method of Claim 17, wherein the antibody is detectably labeled.

20. (Original) The method of Claim 17, wherein the isolated protein is separated by size prior to being contacted with the antibody to MrgX2.

21. (Original) The method of Claim 17, wherein the isolated protein is immobilized on a membrane prior to being contacted with the antibody to MrgX2.

22. (Original) The method of Claim 17, wherein the tissue sample comprises skin cells.

REMARKS

Claims 1-8, 11 and 17-22 are currently pending. Claims 9-10 and 12-16 have been withdrawn pursuant to a Restriction Requirement. Claim 5 has been amended to correct a spelling error. The amendment to the claims adds no new matter.

Paragraphs [0016], [0017], and [0018] of the specification have been amended. Support for the amendments to the specification is found throughout the specification as originally filed. More particularly, support for the amendment to paragraph [0016] is found, *inter alia*, at page 44, paragraph [0183]. Support for the amendment to paragraph [0017] is found, *inter alia*, at page 44, paragraph [0184]. Support for the amendment to paragraph [0018] is found, *inter alia*, at page 44, paragraph [0185]. As a result, the amendments to the specification add no new matter.

No new matter has been added by the foregoing amendments. Applicant respectfully requests entry of the amendments and reconsideration of the application in view of the amendments and the following remarks.

Objection of Drawing

The Examiner objected to the drawings as being unclear. In response, Applicants have amended the Brief Description of the Drawings for Figures 3, 4 and 5. As amended, the Brief Description of the Drawings set forth that Figures 3 and 4 illustrate the expression MrgB1 mRNA as detected by riboprobe, and that Figure 5 illustrates the expression of MrgX2 mRNA in various Wistar Melanoma cell lines. In view of the amendments to the specification, Applicants respectfully request withdrawal of this objection.

Rejections under 35 U.S.C. §§ 101 and 112, first paragraph

Claims 1-8, 11 and 17-22 were rejected under 35 U.S.C. §§ 101 and 112, first paragraph. According to the Examiner, Claims 1-8, 11 and 17-22 are not supported by a specific and substantial or well-established utility and thus the claims lack utility under 35 U.S.C. § 101 and enablement under § 112, first paragraph. More particularly, the Examiner found that because Applicants do not teach whether the levels of MrgX2 protein (as opposed to MrgX2 mRNA) in

the melanoma cells or tissue samples are higher than levels of MrgX2 protein in normal skin tissues, the claimed methods lack utility. Applicants respectfully traverse the rejections.

The claims relate, *inter alia*, to methods of diagnosing skin cancer in a patient involving determining whether cells in a tissue sample from the patient express MrgX2 protein. The Examiner alleges that because Applicants have not shown that MrgX2 protein levels are higher in melanoma cells or tissue as compared to normal skin tissues, one of skill in the art would need to conduct further research to use the claimed methods. *See*, page 5 of the Office Action. The Examiner further alleges that the instant claims lack a specific, substantial, and credible asserted utility because Applicants have not provided "objective evidence that the binding of an antibody to MrgX2 protein (SEQ ID NO: 4) expressed on melanoma tissue or cell is indicative of some skin cancerous condition." *Id.* Applicants respectfully disagree. According to the Examiner, "[m]any proteins are expressed in normal tissues and diseased tissues. Therefore, one skilled in the art needs to know that the MrgX2 protein is present only in diseased tissue to the exclusion of normal tissue or present in the diseased tissues at higher levels or in a different form from that present in normal tissue." Page 5 of the Office Action. Applicants contend the instant specification ***does*** teach that the MrgX2 protein can be present only in diseased tissue to the exclusion of normal tissue. Thus, binding of an antibody is indicative of skin cancer.

The Examiner acknowledges that Applicants teach MrgX2 mRNA is exclusively expressed in melanoma cell lines, and not in other tissues, at Table 2, page 45 and in Figure 5 of the specification. *See*, page 3 of the Office Action. Based on this teaching, one skilled in the art would immediately recognize that if any amount of MrgX2 protein is detected in a tissue sample, that tissue sample ***necessarily*** expressed MrgX2 mRNA, and therefore, must be cancerous. This is because expression of a protein requires that the mRNA encoding the protein be expressed first. Furthermore, one skilled in the art would recognize that because MrgX2 mRNA is ***not*** present in normal tissues and cells, MrgX2 protein ***cannot*** be expressed in normal tissues or cells. Thus, Applicants teach that the MrgX2 protein can only be present in diseased tissue, to the exclusion of normal tissue. As such, Applicants have provided objective evidence that the binding of an antibody to MrgX2 protein expressed on a tissue or cell is indicative of skin cancer.

The Examiner also points out that cells that expressing MrgX2 mRNA may not necessarily express MrgX2 protein, and therefore, the antibody to the protein would not bind to the melanoma tissue or cells. *See*, page 5 of the Office Action. Even if this were to be the case, it would still be true that the binding of an antibody to MrgX2 protein expressed on tissues or cells indicates skin cancer. This is because, as discussed above, MrgX2 protein ***cannot*** be expressed in normal tissues or cells since MrgX2 mRNA is ***not*** present in normal tissues and cells. What is being claimed is a method for identifying skin cancer, ***not*** methods for identifying healthy cells. For example, Claim 1 reads as follows:

> A method of diagnosing skin cancer in a patient comprising:
>
> providing a tissue sample from a patient suspected of having skin cancer; and
>
> determining whether cells in said tissue sample express MrgX2, wherein expression of MrgX2 indicates that the patient has skin cancer.

As recited in the claims, the positive result, i.e., expression of MrgX2, indicates skin cancer. Applicants teach, as discussed above, that the binding of an antibody to MrgX2 protein expressed on a tissue or cells indicates skin cancer. As such, the claims are supported by a specific and substantial or well-established utility.

Claims 1-8, 11 and 17-22 are directed towards methods of diagnosing skin cancer in a patient involving determining whether cells in a tissue sample from the patient express MrgX2 protein. Based on Applicants' disclosure, the skilled artisan would understand that the MrgX2 protein can only be present in diseased tissue to the exclusion of normal tissue. Thus, Applicants have provided objective evidence that the binding of an antibody to MrgX2 protein is indicative of skin cancer, because an antibody to MrgX2 only binds to skin cancer. Therefore, Claims 1-8, 11 and 17-22 are supported by a specific and substantial or well-established utility and thus, the claims have utility under 35 U.S.C. § 101 and enablement under § 112, first paragraph. As such, Applicants respectfully request withdrawal of the rejections.